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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/532,001	03/21/2000	Thomas John Goodwin	MSC-22859-2-CU	7201

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EXAMINER

LACOURCIERE, KAREN A

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

Office Action Summary

Application No.

09/532,001

Applicant(s)

GOODWIN ET AL.

Examiner

Karen A. Lacourciere

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-10,27,28,31-35 and 37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-10, 27, 28, 31-35 and 37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 2, 33, and 35 are objected to because of the following informalities: phosphorothioate has been misspelled as "phosphothiorate". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The rejections of record of claims 1-3, 5-10 and 27 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in response to Applicant's amendments filed 03-17-2003 and December 19, 2003. However, in response to these amendments, new rejections under 35 USC 112, second paragraph, are set forth herein.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-10, 27, 28, and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3, 5-10 27, 28 and 31 are drawn to methods using a transcription factor decoy oligonucleotide, which has been defined in the specification as comprising the binding site for a transcription factor (see for example page 11) and the claims describes the claimed oligonucleotide as a contiguous single

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stranded oligonucleotide that encodes a shear stress response element binding site and the complement of the binding site. It is unclear how a oligonucleotide can be a transcription factor decoy and comprise the binding site, as defined, but actually encode the binding site, as described in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 10 is maintained as rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 10 has been amended to include the limitation, "wherein the concentration of said oligonucleotide is from about 10 nM to about 10 mM". Support cannot be found in the originally filed claims or specification for the limitations "10 nM" and "10mM" and is considered to be new matter.

Applicant has not provided any arguments to traverse this rejection of record.

Claims 1-3, 5-10 27, 28, 31-35 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in

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such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1-3, 5-10 27, 28, 31-35 and 37 have been amended to add new limitations wherein the transcription factor decoy is a single stranded oligonucleotide that encodes a shear stress response element binding site and the complement of the shear stress response element binding site or a nucleic acid encoding such and claim 37 is specifically drawn to a nucleic acid encoding SEQ ID NO:1. No support for these newly added limitations could be found in the originally filed specification or claims. Throughout the originally filed specification and claims, the inventions disclosed is a single strand oligonucleotide comprising a shear stress response element binding site wherein the decoy is directed against a nucleic acid encoding a shear stress response element and its complement, the specification did not disclose or contemplate single stranded decoys which encode a shear stress response element and its complement or nucleic acids encoding such. Although the specification discloses SEQ ID NO:1, the specification does not disclose or contemplate a nucleic acid encoding SEQ ID NO:1. Therefore, these limitations are considered to be new matter.

Response to Amendment

Applicant points to the specification at page 11, lines 10-11 to support the DNA structures newly claimed in the amended claims filed 12-19-2003, however, there is no support for these limitations at this portion of the specification.

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Applicant indicates that the change is merely lexicographic to replace previously amended terminology and does not change the scope of the claim, however, these changes clearly change the scope of the claims, as they require that the specific nucleic acids claimed and used in the methods encode specific shear stress response element transcription factor binding sites.

Claims 1-3, 5-10, 27, 28, 31-33, and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1-3, 5-10, 27, 28, 31-33 and 35 are drawn to methods of inducing expression of a target gene in a cell in culture by contacting the cell with a transcription factor decoy directed against a shear stress response element and decoys comprising single stranded oligonucleotide decoys encoding these shear stress response element binding sites.

The specification provides the structure of one transcription factor decoy (SEQ ID NO: 1, figure 4) targeted to a shear stress response element. The specification also discloses two subsequences, 3'-GAGACC-5' and its complement, 3'-GGTCTC-5', which are preferred embodiments of the shear stress response element. The specification does not provide the sequence of transcriptional factor decoys that up regulate the expression of megalin, cubulin, erythropoietin or 1- α -hydroxylase. The specification does not provide the

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sequence of generally all transcription factor decoys that upregulate the broad genus of genes which are renal tubular epithelial specific genes or upregulate the genus of genes involved in the production of 1,25-dihydroxy-vitamin D3. Claims 1-3, 5-10, 27, 28, 31-33 and 35 encompass decoy oligonucleotides that encode a shear stress response element from any cell type or organism and SSRE transcription factor binding site sequences which regulate the expression of a wide variety of genes. The sequence of this broad genus of SSRE transcription factor binding site sequences would be required to envision the broad genus of single stranded nucleic acids encoding the broad genus, however, Applicant has not disclosed a sufficient number of species of this broad genus, such that the skilled artisan would recognize the inventor was in possession of the broad genus of nucleic acid decoys encoding SSRE transcription factor binding site sequences encompassed in the claims, or required to practice the claimed methods. Multiple SSRE elements exist, not all of which comprise the one structural element described in the specification (the sequence 3'-GAGACC-5', or its complement). For example, Ando et al. (Jpn Heart J., Vol. 37, No. 1, Jan. 1996, p19-32) indicate that numerous SSRE appear to exist and note that genes up regulated by shear stress do not require a 3'-GAGACC-5' sequence (see for example, Ando et al., page 27, second paragraph). Additionally, the claims encompass decoy oligonucleotides comprising 3'-GAGACC-5' or 3'-GGTCTC-5' and further comprise flanking sequences which are specific to particular gene targets, which have not been described in the specification or the prior art. None of these sequences meet the written description provision of 35 USC 112, first

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paragraph. The specification provides insufficient written description to support the genus encompassed by the claim, because the genus is very broad and highly variant with regard to structure (i.e. nucleotide sequence). The one decoy sequence, SEQ ID NO:1, and the subsequence 3'-GAGACC-5' and its complement, 3'-GGTCTC-5', would not provide sufficient written description to determine the structure, i.e. nucleotide sequence, or the full genus of sequences encompassed in the claims. For example, the specification has not described any other SSRE decoy sequence, nor has it described the structure, i.e. nucleotide sequence, for the flanking sequences that would be required for all decoy oligonucleotides comprising 3'-GAGACC-5' and its complement, 3'-GGTCTC-5', nor has the specification described the sequences for SSRE's that regulate expression of megalin, cubulin, erythropoietin or 1- α -hydroxylase or transcription factor decoys that upregulate the broad genus of genes which are renal tubular epithelial specific genes or upregulate the genus of genes involved in the production of 1,25-dihydroxy-vitamin D3.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

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Therefore, only SEQ ID NO: 1, but not the full breadth of the claim, meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Response to Arguments

Applicant's arguments filed 12-29-2003 have been fully considered but they are not persuasive. In response to the Office action mailed 09-23-2002, Applicant presents arguments, without clearly stating what rejections are being addressed by these arguments, however, these arguments have been considered to the extent they appear to address the basis of the rejections set forth in the instant Office action.

Applicant argues that Ando et al. (cited in the rejection under 35 USC 112, first paragraph, lack of adequate written description) speculate on the sequence and importance of an SSRE, but do not teach the use of SSRE's for modulating transcription factor activity and argue that the use of a single ODN to deliver and modulate the transcription factor activity is novel. These argument do not appear to address the lack of written description, as they appear to comment on the novelty of the invention in view of Ando et al., however, Ando et al. has not been cited in an art rejection. Ando et al. support the written description rejection by supporting the assertion that the genus of SSRE's, required by the claims, is broad and variable and was not described by the art at the time of the invention.

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Although Applicant argues that the specification has demonstrated that the SSRE can modulate certain genes, this also does not address the basis of the rejection, which concerns written description. Although the Applicant describes one decoy sequence, this sequence would not describe the full genus of sequences claimed or required for the claimed methods, as discussed in the rejection of record.

Although one sequence with the properties was described in the specification, as discussed by applicant, this one sequence would not be sufficient to describe the broad genus of sequences required by the claims.

The rejections of record of claims 1, 5, 7, 8 and 10 under 35 U.S.C. 102(b) as being anticipated by Khachigian et al. and claims 1-3, 5, 7, 8, 10 and 27 under 35 U.S.C. 103(a) as being unpatentable over Dzau et al. (WO 95/11687) in view of Khachigian et al. and Goodwin et al. are withdrawn in response to Applicant's amendments.

Applicant's arguments directed to Dzau et al. and Khachigian et al. do not appear relevant to the rejections set forth in the instant Office action.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (571) 272-0759. The examiner can normally be reached on Monday-Thursday 7:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Lacourciere
March 22, 2004


KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER